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P01/7700 0.00-0220312.3

Request for grant of a patent

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1. Your reference	srt.1886.uk.cr.d	
2. Patent application number *(The Patent Office will fill in this part)*	31 AUG 2002	0220312.3
3. Full name, address and postcode of the or of each applicant *(underline all surnames)* 08456410001 Patents ADP number *(if you know it)* If the applicant is a corporate body, give the country/state of its incorporation	Professor Neil Graham 6 Kilmardinny Grove Bearsden GLASGOW G61 3NY	
4. Title of the invention	Novel thermoplastic hydrogel polymer compositions for use in producing contact lenses and methods of producing said compositions	
5. Name of your agent *(if you have one)* "Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)* Patents ADP number *(if you know it)*	Kennedys Patent Agency Limited Floor 5, Queens House 29 St Vincent Place GLASGOW G1 2DT 08058240002	

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7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application	Number of earlier application	Date of filing *(day / month / year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:* *a) any applicant named in part 3 is not an inventor, or* *b) there is an inventor who is not named as an applicant, or* *c) any named applicant is a corporate body.* *See note (d))*	No

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Continuation sheets of this form	
Description	11
Claim *(s)*	
Abstract	
Drawing *(s)*	1 + 1

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Priority documents	
Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. I/We request the grant of a patent on the basis of this application.

Kennedys

Signature KENNEDYS

Date 30 August 2002

12. Name and daytime telephone number of person to contact in the United Kingdom

Claire Rutherford 0141 226 6826

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Novel Thermoplastic Hydrogel Polymer Compositions for use in producing contact lenses and Methods of Producing said Compositions

The present invention relates generally to production of thermoplastic hydrogels for use as contact lenses. In particular, the invention relates to thermoplastic hydrogels which show improved flow characteristics.

It is already known in the art to make contact lenses using hydrogels. Generally these hydrogels are HEMA, NVP or products of free radical polymerisation. However, these compositions generally do not flow and can only be moulded by reaction injection moulding (RIM), which is a slow and relatively expensive process which is not particularly suited to contact lens manufacture.

Also, existing reaction injection moulding techniques utilise free radical initiation or irradiation cure that produces radicals. These radicals initiate a peroxidation chain process, which leads ultimately to damage of PEO based polymers in storage for use which gives a short life to contact lenses produced from them.

There are also problems with bio-compatibility of reaction injection moulded hydrogels which again is not ideal for the manufacture of contact lenses where bio-compatibility is importantant.

Additionally, the current cross linked polymer hydrogels often have a very poor resistance to crack initiation and crack propagation which again can be problematic when producing contact lenses.

It can therefore be seen that it would be beneficial to provide thermoplastic hydrogels which are capable of being generally moulded under pressure so that contact lenses can be easily and cheaply produced.

It is an aim of the present invention to provide a thermoplastic hydrogel composition which has the ability to flow under moderate shear at particular temperatures below the polymer decomposition temperature.

It is a further object of the present invention to provide a thermoplastic hydrogel composition which can be injection or compression moulded.

It is a further object of the present invention to provide a solvent soluble composition.

Another object of the present invention is to provide a thermoplastic hydrogel composition which is highly bio compatible.

A yet further object of the present invention is to provide thermoplastic hydrogels which have a high level

of water swelling properties after moulding and swelling with water.

According to a first aspect of the present invention, there is provided a method of producing thermoplastic hydrogels for use in producing contact lenses, comprising the steps of reacting one or more from the list;

polyethylene oxide,
polyol,
polyamine,

with a polyisocyanate and a polyfunctional amine or alcohol.

Preferably the polyol is polyethylene glycol.

Preferably, the method also comprises the step of end capping unreacted groups with a unit capable of producing hydrogen bonding, π bonding, ionic boding and/or phase separation or forming a glassy phase separated domain.

Alternatively, according to a second aspect of the present invention, the method also comprises the step of end capping unreacted groups with a unit from a list of:

Mono-functional amine
Mono-functional isocyanate
Monofunctional anhydride
Acid
Mono-functional hydroxyl

Preferably the reaction between one or more from the list

polyethylene oxide
polyol
polyamine

and a polyisocyanate is prepared using a range of NCO:OH or NCO:NH_2 ratios.

Optionally a biodegradable unit may be incorporated.

The biodegradable unit may be polycaprolactone, poly (lactic acid), poly(glycolic) acid or poly(hydroxybutyric)acid, amine or hyroxyl ended poly(amino) acids (protein or peptide analogues).

The ratios are preferably selected such that, at complete reaction, the product does not form a macrogel.

Preferably the first step reaction is prepared using a range of NCO:OH OH or NCO:NH_2 ratios from 2:1 to 1:2.

Most preferably the first step reaction is prepared using NCO:OH OH or NCO:NH_2 ratios of 2.0:1 to 1:1.8 and 1.8:1 to 1:1.8.

Optionally the range of ratios used may be extended by the addition of monofunctional amines, alcohols or cyanates.

Alternatively, a macrogel is prevented from forming by stopping the reaction before completion.

Preferably, the reaction is stopped by the addition of a monoamine or an amine terminated polymer.

Optionally, the monoamine or an amine terminated polymer is added when the reaction is partially complete.

Alternatively, an amine is admixed at the outset thus removing the possibility of gelation.

Preferably, the amine is added in the form of amine carbonate.

Typically, products with NCO end groups are subjected to a final curing by immersion in liquid water or steam after moulding.

Preferably, in the second stage the unreacted groups are capped with an amine.

Optionally, unreacted NCO groups are endcapped.

Another option is that unreacted OH groups are endcapped.

Preferably, terminal NCO groups are converted into a strongly hydrogen bonding urea group.

Preferably, the unreacted groups are capped with an aliphatic amine.

Optionally, the amine group is attached to a long linear or branched alkyl group or to an aryl- or aralkyl-amine.

Optionally, the amine group is attached to polymers or low molecular weight pre-polymers.

Alternatively, excess OH groups are capped with one or more molecules from the list of;
mono-isocyanate ended aromatic molecules,
mono-acid anhydride ended aromatic molecules,

mono-isocyanate ended aliphatic molecules,
mono-acid anhydride ended aliphatic molecules
reaction product of a monoamine with a di(or higher) isocyanate.

The groups used in the endcapping process allow the polymers to interact with physical or chemical cross-linking. The separate particles therefore bind to each other.

According to the third aspect of this invention there is provided a thermoplastic hydrogel for use in producing contact lenses produced by the methods of the first and second aspects.

Preferably, the hydrogel is completely polymerised under the specific conditions that are being used.

Preferably, after polymerisation the hydrogel is heated.

Alternatively, after polymerisation the hydrogel is immersed in water liquid or vapour.

Optionally, the end product may be pelletised, pressed, extruded or heat, pressure, injection or compression moulded.

Preferably, the end product incorporates an antioxidant containing two or more hydroxyl groups.

The antioxidant may be internal or external.

Preferably, the antioxidant is ascorbic acid.

Alternatively, the antioxidant is 2,6-ditertiarybutyl4-hyroxanisol.

Optionally, the end product can incorporate dye.

According to a fourth aspect of the present invention there is provided a contact lens produced from the hydrogel of the third aspect.

An example of the present invention will now be illustrated by way of example only and with reference to the following figure, in which:

Figure 1 shows typical end groups that could be envisaged as being associated in stacks as shown.

In the preferred embodiment, the thermoplastic materials are prepared from mixtures of di (or higher) PEG polyol with a di (or higher) polyisocyanate and/or a di (or higher) polyamine.

First stage materials can also be made from many step-growth reactions amongst which the reaction of PEG polyols with polyacids with removal of reactive-produced water is an option. The production of first stage materials can also be guided by the art of making alkid resins in the paint industry.

If the product from the first stage reaction is made from a mixture of PEG diol, 1, 2, 6-hexantriol and diphenylmethane-4,4-diisocyanate, it can be prepared using a range of NCO:OH ratios from, for example, 2:1 to

1:2. At the extremes of these ratios, the 2:1 will have all NCO unreacted groups and the 1:2 ratio will have all OH unreacted groups. These compositions are not able to macrogel and will contain only small proportions of low molecular rate branched polymers. The product is a fluid and suitable for injection, extrusion or compression moulding at temperatures which are typically below 150°C, although temperatures of 200°C to 250°C can be utilised for short periods. It should be noted that the products with NCO end groups can only be moulded and subjected to final curing by immersion in liquid water or steam for a suitable period.

It is possible to use intermediate NCO:OH ratios, such as 2:1 to 1:1.8 and 1.8:1 to 1:1.8 (and these ranges can be further extended by the addition of mono-functional molecules). As these still provide at complete reaction, fluid systems, which when the end groups, are NCO can be injection moulded and post-cured by water or steam immersion. However, depending on the proportion of tri or higher functional materials, ratios such as 1.6:1 to 1:1.6 form macrogels at as complete a reaction as is possible with the NCO and OH groups present (and less extended ratios are possible if mono-functional amines, alcohols or cyanates are used in the first stage. The resulting products are not fuseable and are not solvent soluble). It is possible that the products may still be used for the second stage of the process, to give useful end capped products, if the reaction is stopped before it has proceeded as far as possible. This operation is less convenient and more difficult as the degree of completion of the reaction must be determined using, for example, infra-red analysis of the isocyanate absorption peak of

the reaction mixture, or by the viscosity of the reaction. Therefore, it is much preferred to use the compositions which cannot macrogel, as they can be taken to completion of the first stage without fear of irreversibly solidifying the reactants.

A preferred embodiment is that the first stage product is a heavily branched polyurethane/PEG resin. In this embodiment, the second stage is intended to convert each of the terminal groups into a strongly hydrogen bonding urea group. An aliphatic amine could be used and the amine group could be attached to a short or long linear or branched (preferably linear) alkyl group, such as decyl or stearic or higher polyamines such as polyethylene, or to an aryl or aralkylamine, such as aniline, aminoanthracene or octylaniline. The combination of the urea group and the long aliphatic chain or aromatic ring will promote association and phase separation of these groups with development in the product material of toughness and strength. This will be especially the case where an aromatic diisocyanate has been utilised in stage one.

Figure 1 shows a diagram of a typical end group which could be envisaged as associating in stacks, as shown. The association of many such end groups should provide increased cohesion and strength to the product.

Once the initial homogeneous mixing has been completed, then the still fluid mix may be poured into suitable containers, such as polypropylene moulds. The polymerisation (curing) of the finished product can then be completed. In order to provide an oxidation resistant

product, it is particularly useful to incorporate a reactive antioxidant containing two or more hydroxyl groups, for example, ascorbic acid (alternatively an external anti-oxidants may be used). Alternatively the antioxidant may be added in earlier during the first stage.

The final product can then be moulded into contact lenses. The product has a number of benefits, in particular as there will be no unreacted extractable groups left in the completed product, it is particularly useful for contact lenses as it is bio-compatible. There is also the benefit that materials made from the final hydrogel product which are soft and strong would be comfortable and re-useable again something which is particularly useful in contact lens manufacture. The final product would also have the benefit of being intrinsically rubbery in their dry state, and therefore contact lenses would not set rigid when dried out. Also, coloured dyes can be put into the final product easily, which cannot be done with similar cross-linked hydrogels and this could be useful when making "fashion" contact lenses, or sun protective or prosthetic contact lenses which have colours, designs or dyes with particular characteristics incorporated into them.

It can be seen that the embodiments disclosed are both or merely exemplary of the present invention, which may be embodied in many different forms. Therefore, details disclosed herein are not to be interpreted as limiting, but merely as a basis for the claims and for teaching one skilled in art as to the various uses of the present invention in any appropriate matter. In particular, it

should be noted that a wide variety of changes can be made in this process.

For example, pre-polymers with excess OH can be capped with a mono-isocyanate ended aromatic or aliphatic molecule or with a reaction product of a mono-amine with di or higher isocyanate. The low molecular weight amine could be replaced with a low molecular weight polymeric amine, such as low M_n primary and secondary amine ended nylon polyamide) or polypropylene oxide, poly(butanediol) or low molecular weight polymers producing glassy domains such as end-capped polystyrenes or amine end-capped hydrophobic and crystalline domain forms such as poly(ethylene) units. The reaction can be between such amine ended PEGs and PPGs and di or higher amines and di or higher isocyanates, but done in solvents to allow suitable reduced viscosity to be obtained. Also, to slow down the amine reaction, the amine can be added at the outset as the carbonate version of amine carbonate, resulting from the reaction of amine and carbon dioxide.

Also, stage one hydroxlic excess polymers could be reacted with a phase separating polymer end capped with an anhydride group.

Finally, it should be noted that this end capping process could be applied to a wide variety of polymers, such as polyesters, nylons, polyurethanes, polyureas, polyethers, polyolefins, polyvinyls and poly(meth)acrylates.

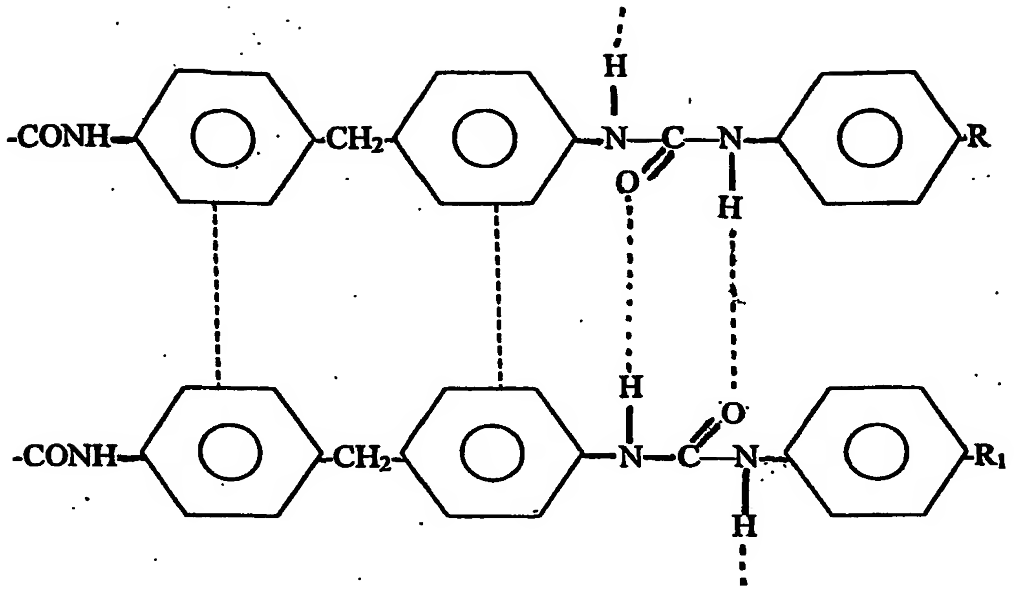

Fig 1

PCT Application

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